HYPERGLYCAEMIC NONKETOTIC COMA IN DIABETES, OCCASIONED BY A CONCENTRATED CARBOHYDRATE DRINK

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THE CASE is reported because it suggests that hyperglycaemic nonketotic coma may be caused in certain diabetic persons by the ingestion of a large quantity of carbohydrate. The coma or stupor is exogenous, and not endogenous. The disease is an example of true food poisoning.

The patient was a widow of seventy-four who lived alone. Her husband had died a few months earlier. She had been ill at home for some four weeks or more. She was found unconscious in her house. At the time of admission she was stuporose. She had been weak. She had been very thirsty and had drunk a lot. She had eaten less and less. From time to time she had vomited. In spite of drinking, the thirst had increased. Her legs became so weak that she could hardly walk.

On examination, besides the impairment of consciousness, there was dehydration. She felt cold, and the rectal temperature was 96.8°F. There was no tremor, flap or convulsive movement. There was no hyperventilation of a ketotic kind. No ketones were found in the urine, though it was tested many times. The skin was depigmented. There were Heberden's nodes. There was trunk obesity. It was later evident that she was deaf, and that there was impairment of vision. The haemoglobin was 86 per cent. The biochemical findings are set out in Table I. The clinical and biochemical features seem to establish a diagnosis of diabetes mellitus, with extreme hyperglycaemia, dehydration, and stupor or semi-coma, but without ketosis.

It can be seen from Table I that a good result was obtained by treating the patient with insulin, and with intravenous infusion of water, and with electrolyte adjustment. Our patient was stabilised in convalescence on a diabetic diet of 1,500 calories and the Tablet of Tolbutamide, B.P. Evidently in this disorder the cerebral depression is reversible, because the patient returned to her normal state of alertness and ability.

We already knew that occasionally, when a patient, not yet recognised to be diabetic, first comes for examination, the initial blood sugar levels may be higher than the severity of the diabetes mellitus would warrant. We also knew that this has been because the thirsty patient has been taking a concentrated carbohydrate drink (C.C.D.). These flavoured, coloured, carbonated carbohydrate drinks have become very popular since they became available some years ago. They are drunk in Belfast as lemonade and other "minerals" are, and it has passed into the folk-lore of the city that they are sources of nourishment and strength. The composition of the two common concentrated carbohydrate drinks (C.C.D.1. and C.C.D.2.) are set out in Table II and Table III. C.C.D.1. is the more popular, and its satiety value is low. Another of our diabetic patients drank a bottle (25 fluid ounces – 710 ml.) in one and a half hours, and could have drunk more if it had been to hand. For the composition of Liquid Glucose (B.P.C.1963) see Table IV. It will surprise many that Liquid Glucose is not a solution of dextrose. Of its solids four-fifths are complex

DATE	TIME	BLOOD SUGAR mgm%	INSULIN DOSE	Na.	K.	Cl.	CO_2CP	P.S.G.	UREA	pH	pCO_2	BASE EXCESS	BUFFER BASE	STANDARD BICARBONATE	WATER INTAKE	URINE OUTPUT
24th JAN	5.30pm	1040	400 UNITS INSULIN B.P.	140	5.0	104	14.4	1.031	40						180 fluid ounces (5112 ml.)	12 fluid ounces (340 ml.)
	7.45pm	1060		140	3.3	108										
	10.00pm	810		148	3.0	114		1.028	45	7.32	21.5	-13.0	38.2	15.2		
25th JAN	12.45am	460	416 UNITS INSULIN B.P.	150	3.6	116										
	7.30am	70		138		106	16	1.034	148							
	8.45am	60		154	4.0	116	27	1.024	127						131 fluid ounces (3720 ml.)	26 fluid ounces (738 ml.)
	11.00am	62		155	3.9	114	26	1.023	128	7.37	32.5	-5.2	44	20		
	3.00pm	380		140	4.5	111	30	1.022	132							
	11.00pm	550		141	4.9	103	28	1.023	130							
26th JAN	10.30am	280	80 UNITS INSULIN B.P.	142	4.8	107	24	1.022	108	7.5	25	-1.6	48	22.6	151 fluid ounces (4288 ml.)	73 fluid ounces (2073 ml.)
	4.00pm	212		137	4.4	105	25	1.022	93							
	10.45pm	330		139	4.8	106	24	1.021	78							
27th JAN	am	320	136 UNITS INSULIN B. P.	136		107	21	1.022	49	7.39	34	-3.8	45	21.1	123 fluid ounces (3493 ml.)	98 fluid ounces (2783 ml.)
	12 noon	292														
	5.00pm	304		135	4.8	110	22	1.022	37							
28th JAN	12 noon	292	140 UNITS GLOBIN ZINC INSULIN B.P.	139	5.0	107	21	1.023	46							
	5.00pm	138														
	9.30pm	30														
29th JAN	7.00am	30	140 UNITS GLOBIN ZINC INSULIN B.P.													
	10.45pm	25		139	3.8	112	19	1.022	37							

Table I.

TABLE II

Composition of Concentrated Carbohydrate Drink 1 – Manufacturer's information

Each bottle contains in 25 fluid ounces (710 ml.):

Liquid Glucose (B.P.C.1963)	26.5% w/v
Citric acid	0.2% w/v
Lactic acid	0.1% w/v
Sodium benzoate	0.03% w/v
Flavouring	
Colouring	
Totals in bottle	
Liquid Glucose	185.0 grams
Lactic acid	.7 gram
Citric acid	1.4 gram
Sodium benzoate	.21 gram

If the total carbohydrates in a bottle are calculated as monosaccharides, the result is equivalent to 155 grams of glucose.

For the composition of Liquid Glucose (B.P.C.1963) see Table IV.

TABLE III

Composition of C.C.D.2. – Manufacturer's information

Each bottle contains in 25 fluid ounces (710 ml.):

Liquid Glucose B.P.C.	28.0% w/v
Citric acid	.08% w/v
Tartaric acid	.14% w/v
Saccharin	.007% w/v
Sodium benzoate	598 p.p.m.
Total Liquid Glucose in bottle	198 grams
Total carbohydrate in bottle	163 grams

TABLE IV

Composition of Liquid Glucose (B.P.C.1963)

The monograph in the British Pharmaceutical Codex 1963 states that Liquid Glucose is a colourless or almost colourless, very viscous syrup, produced by the hydrolysis of starch, containing dextrose (10–20%), dextrins, maltose and water.

The manufacturers of C.C.D.1. state that in 100 grams of Liquid Glucose solids there are the following:

Dextrose	19.3 grams
Maltose including isomaltose	14.3 grams
Trisaccharides	11.8 grams
Tetrasaccharides	10.0 grams
Pentasaccharides	8.4 grams
Hexasaccharides	6.6 grams
Heptasaccharides	5.6 grams
Octa – and higher saccharides	24.0 grams
Total	100.0 grams

Liquid Glucose is not included in the British Pharmaceutical Codex 1968.

saccharides, and only one-fifth is dextrose. Syrup of Liquid Glucose is a different preparation – 33 per cent w/w of Liquid Glucose in Syrup B.P. (which itself is Sucrose B.P. 66.7 per cent w/w in water).

As soon as our patient could answer questions we asked her what she had been drinking to quench her thirst. She said she had been drinking C.C.D.1., and also in a lesser quantity C.C.D.2. She had drunk a bottle (25 fluid ounces – 710 ml.) every day, or every two days, and the more she drank the thirstier she became. It will be seen from Table II that one bottle of C.C.D.1. would add the equivalent of 155 grams of glucose to her daily intake, and, from Table III, one bottle of C.C.D.2. would add 163 grams of carbohydrate. We do not know how many bottles of C.C.D.1. the patient really drank in the day, but the satiety value is low, and there would be no difficulty in taking several bottles a day. C.C.D.2. is sweeter to taste, and it is not so easy to take several bottles daily.

Our interpretation of the case is that our patient was an elderly mild diabetic, of a type not likely to be, or to become, ketotic. Her pattern of eating was upset by the death of her husband, and the consequent living alone. She became thirsty, and to relieve the thirst drank, among other things, C.C.D.1. and in a lesser quantity C.C.D.2. This substantial increase in carbohydrate intake promoted extreme hyperglycaemia, and a glucose diuresis. In consequence there was dehydration (made worse in the end by vomiting) and a fall in plasma volume. This resulted in poor organ and tissue perfusion, and in general metabolic failure. We take the hypothermia to be a feature of failing metabolism, and we take the initial low blood urea to be evidence of depressed liver function. We suppose the rise of blood urea, when the patient was treated and improved, to mark an improvement in liver function. Conversely the original high level of blood sugar may have been in part due to failure of the liver to take up glucose.

We suggest, therefore, that hyperglycaemic nonketotic coma in diabetes may be due to a diabetic person, of a type who is not likely to become ketotic, and who does not know that he or she is diabetic, becoming thirsty, and then consuming large quantities of C.C.D. If the thirsty phase is caused by infection or gangrene, the outcome may not be so favourable as in our case, where there was no infection and no gangrene.

It is in accord with this view that Lucas (1963) reported that his first case "had an intense craving for glucose-containing beverages for several weeks before admission" and that "as a result, his daily intake of carbohydrate was often several hundred grammes higher than the average".

Polydipsia is a more common and compelling diabetic symptom than polyphagia, so the syndrome is more likely to be produced by carbohydrate drinks than by solid carbohydrate foods. Nevertheless, solid carbohydrate foods can produce the syndrome in nondiabetics (Rosenberg *et al.*, 1965), and in diabetics as recorded by White (1963) and perhaps by Halmos (1966). Halmos' case 3 had "a craving for sweets" before becoming drowsy with a blood sugar of 1210 mg/100 ml. White reported that his patient "consumed exceedingly large quantities of cake, confections, and ice-cream, and became ill shortly before her admission to hospital with gastro-enteritis after consuming raspberry syrup".

It supports our view of the causation that a similar hyperglycaemic nonketotic coma is seen in forced feeding of burned patients (Rosenberg *et al.*, 1965). This coma occurred in burned patients, who were fed very large quantities of carbohydrate, so as to give them a high calorie intake. Rosenberg mentions calorie intakes of up to 6,000 a day, and carbohydrate intakes of up to 1,000 grams a day. These patients had blood sugars from 800 to 1,600 mg/100 ml. Of six patients three survived. Of these three, in convalescence, only one had a mildly diabetic glucose tolerance test.

It further supports this view that the syndrome in diabetic patients almost always occurs *before* diabetes mellitus is diagnosed, and not often afterwards. Probably patients, once they know that they are diabetic, and once they have been instructed in dieting, do not take C.C.Ds. and so do not have the syndrome.

It seems that the syndrome may occur not only in nondiabetic persons, and in mildly diabetic persons, but also in persons with pancreatitis (Davidson, 1964; Halmos, 1966 – Case 6; Ward, 1963). Perhaps it occurs in pancreatitis because of pancreatic diabetes, and a high carbohydrate load in drinks and infusions.

When, because of diabetic thirst, or for any reason, the protection of the satiety mechanism has been overcome, and an excessive and harmful carbohydrate load has been ingested, no further protection is afforded by restraint in absorbtion. The small intestine can absorb up to one gram of glucose per kilogram body weight per hour (Hoffman, 1964).

The first report of this syndrome is usually taken to be that of Sament and Schwartz (1957) though extreme hyperglycaemia had often been reported before. The first Belfast report was that of Grant (1965). The second Belfast report was that of Halmos *et al.* (1966). C.C.D.1. was first distributed in Belfast in 1950. It first was manufactured in Belfast in 1953. It became popular immediately, because it was an agreeable drink for well people, and a useful form of water and glucose for sick people. Indeed it is a helpful advance in materia medica. However, it seems that its inappropriate use has produced a disorder new to us. It is interesting that at one time the Liquid Glucose content of C.C.D.1. was increased by 28 per cent w/v, but it was found that at that strength "it was not thirst-quenching" – "people had to go back for more".

It is worth remembering that there is a third concentrated carbohydrate drink, used in renal failure, not directly on sale to the public, which contains 106 grams of carbohydrate in each bottle of 175 ml. (6 fluid ounces). Renal units using this drink should know of the risk of inducing hyperglycaemia.

An analogous risk of hyperalimentation may be seen in tube feeding, when, if too much protein is administered, uraemia may be induced (Engel and Jaeger, 1954). In this case too, the normal mechanism of satiety no longer protects the patient against an excessive and harmful intake of a food constituent. In each case, there is true food poisoning.

It is possible that co-existing hyperglycaemic *and* ketotic comas may be seen. The case of Argy (1925) may illustrate this. It is no doubt important not to induce an element of hyperglycaemic coma, when treating diabetic ketotic coma, by infusing intravenously unnecessary quantities of dextrose solution.

Treatment should begin with stopping the abnormal carbohydrate intake, if it has not already ceased. It ought to continue with the Injection of (Soluble) Insulin B.P. and the intravenous infusion of water. An important question is, in what form should the water be infused? It is plainly not at first appropriate to use dextrose solutions.

In the early stage of treatment, when the plasma is hyperosmolar, all solutes seem contraindicated. There seems to be no contraindication to the infusion of Water for Injection B.P. in 500–ml. units. Some failures and difficulties in treatment in these cases may have been due to a reluctance to infuse Water for Injection B.P. There seems no danger in the first stage of treatment of producing hypo-osmolarity of the plasma, nor of producing red cell haemolysis. After the first hour it will likely be necessary to use a potassium solution, and Sterile Potassium Chloride Solution B.P. 10 ml. (or more, or less, as the need may be), may be added to 500 ml. of Water for Injection B.P. and infused. The addition of 10 ml. makes a 0.3 per cent solution of potassium chloride. A 1.19 per cent solution is iso-osmolar. Progress is not difficult to monitor, if one observes pulse volume, blood pressure, urine output and venous pressure, and has frequent estimations of blood sugar and of electrolytes and urea. When these estimations indicate it, solutions of sodium chloride or of dextrose or of sodium bicarbonate may be infused, iso-osmolar or hypo-osmolar as the need is.

The acidosis may need no special treatment and it may be better not to include sodium bicarbonate solution in the intravenous programme at least in the beginning. Increase in osmolarity is to be avoided.

If there has been a period of some weeks of malnutrition, it seems proper to administer Injection of Thiamine Hydrochloride, B.P. 25 milligrams, Injection of Nicotinamide, B.P. 100 milligrams, and Injection of Hydroxocobalamin, B.P. 1,000 micrograms, so that deficiency of these will not persist, and delay improvement, especially in the central nervous system.

Summary

The introduction of palatable, concentrated, carbohydrate drinks, particularly of those of low satiety value, has increased the number of cases of hyperglycaemic, nonketotic coma in diabetic persons. As proposed by White (1963), the severity of the hyperglycaemia and of the coma depends mainly on the size of the ingested carbohydrate load, and not on any peculiar severity of the diabetic process. The ingested load is high because the ordinary mechanism of satiety is not operating to keep the load in normal limits. This may be because the carbohydrate preparation has a low satiety value (e.g. C.C.D.1.), or because the normal mechanism has been overcome by diabetic polydipsia or polyphagia, or because some neurological lesion has depressed the satiety centre, or because of forced therapeutic over-feeding as in burned patients.

Both concentrated carbohydrate drinks and dextrose infusions should be used with caution in pancreatitis. Dextrose infusions should be used with caution in treating diabetic ketotic coma.

Treatment of hyperglycaemic nonketotic coma may include Water for Injection B.P. in the early stage. Unless there is some special indication, sodium chloride solution, dextrose solution, and sodium lactate and bicarbonate solutions should not be used while hyperosmolarity is still present.

Acknowledgements

We are indebted to Mr. Desmond Neill, consultant biochemist, for the biochemical estimations.

We are grateful to Sister J. Montgomery for the use of the nursing record.

Doctor B. T. McNamee made the diagnosis in the admission unit.

We are grateful to Miss M. Gribbon for her patience and care in typing the manuscript.

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